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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,726	12/08/2005	Renyuan Bai	K21788USWO (C038435/01953)	3759
7590	10/16/2007	Stephen M Haracz Bryan Cave 1290 Avenue of the Americas New York, NY 10104	EXAMINER SWOPE, SHERIDAN	
			ART UNIT 1652	PAPER NUMBER PAPER
			MAIL DATE 10/16/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,726	BAI ET AL.	
	Examiner	Art Unit	
	Sheridan L. Swope	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 09 August 2007.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 5-7, 17 and 18 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-4, 8-16, 19, and 20 is/are rejected.
- 7) Claim(s) 1-4, 8-16, 19 and 20 is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 08 December 2005 is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>1205</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's election of Invention I, and SEQ ID NO: 1 with mutation at Ile¹⁷, in their response of August 9, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 1-20 are pending. Claims 5-7, 17, and 18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 1-4, 8-16, 19, and 20 are hereby examined.

Priority

The priority date granted for the instant invention is June 12, 2003, the filing date of EPO 03012294.9, which disclosed the elected invention.

Drawings-Objections

The drawings are objected to for disclosing sequences that are not identified by a sequence identifier number (SEQ ID NO:). The sequence rules embrace all amino acid sequences with four or more amino acids. Said sequences must be disclosed in a sequence listing and identified by a specific SEQ ID NO: (MPEP 2421.02). 37 CFR 1.821(d) requires the use of the assigned sequence identifier number in all instances where the description or claims of a patent application discuss sequences, regardless of whether a given sequence is also embedded in the text of the description or claims of an application. Applicant is required to check the disclosure completely and to make corrections to identify all of the sequences disclosed therein by sequence identifier numbers.

Claims-Objections

Claims 1-4, 8-16, 19, and 20 are objected to for reciting non-elected subject matter.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-4 and 8-16 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The modified mevalonate kinases of Claims 1-4 and 8-10, the polynucleotides of Claims 11-14, and the host cells of Claims 14-16 are likely to occur in nature and, therefore, the recited products do not show the “hand of man”.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-4, 8-16, 19, and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the following reasons.

Each of Claims 2-4, 8-16, 19, and 20 are indefinite due to improper antecedent usage, as follows. For Claims 2-4, 8-12, and 19, the phrase “A [a] modified mevalonate kinase according to claim...” should be corrected to “The [the] modified mevalonate kinase according to claim...”. For Claims 12 and 13, the phrase “A [a] polynucleotide according to claim 11” should be corrected to “The [the] polynucleotide according to claim 11”. For Claim 14, “A vector or plasmid according to claim 13” should be corrected to “The vector or plasmid according to claim

13". Claim 15, as dependent from Claim 13, is indefinite for the same reason. For Claim 16, "A host cell according to claim 15" should be corrected to "The host cell according to claim 15".

For Claim 20(d), the phrase "the polynucleotide" renders the claim indefinite. It is unclear whether said phrase refers to the polynucleotide encoding the first or second mevalonate kinase. For purposes of examination, it is assumed that said phrase refers to the polynucleotide encoding the second, modified mevalonate kinase.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 1-4, 8-11, 13-16, 19, and 20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polypeptide of SEQ ID NO: 1 having an Ile¹⁷Thr substitution, does not reasonably provide enablement for any variant of SEQ ID NO: 1, having any structure comprising a substitution at Ile¹⁷, and having melavonate kinase activity with decreased feedback sensitivity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In regards to this enablement rejection, the application disclosure and claims are compared per the factors indicated in the decision In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). These factors are considered when determining whether there is sufficient evidence to support a description that a disclosure does not satisfy the enablement requirement

and whether any necessary experimentation is undue. The factors include but are not limited to:

(1) the nature of the invention; (2) the breadth of the claims; (3) the predictability or unpredictability of the art; (4) the amount of direction or guidance presented; (5) the presence or absence of working examples; (6) the quantity of experimentation necessary; (7) the relative skill of those skilled in the art. Each factor is here addressed on the basis of a comparison of the disclosure, the claims, and the state of the prior art in the assessment of undue experimentation.

Claims 1-4 and 8-10 are so broad as to encompass any variant of SEQ ID NO: 1, having any structure comprising a substitution at Ile¹⁷, and having melavonate kinase activity with decreased feedback sensitivity. The scope of each of these claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claim. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired melavonate kinase activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, in this case the disclosure is limited to the amino acid sequence of SEQ ID NO: 1 having an Ile¹⁷Thr substitution.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims. Furthermore, the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited

in any protein and the results of such modifications are unpredictable (Galye et al, 1993; Whisstock et al, 2003). In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of Claims 1-4 and 8-10, which encompasses all variants of SEQ ID NO: 1, having any structure comprising a substitution at Ile¹⁷, and having melavonate kinase activity with decreased feedback sensitivity. The specification does not support the broad scope of Claims 1-4 and 8-10 because the specification does not establish: (A) regions of the protein structure which may be modified without affecting the melavonate kinase activity or decreased feedback sensitivity; (B) the general tolerance of the melavonate kinase activity or decreased feedback sensitivity to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Since Claims 11, 13-16, 19, and 20 further recite polynucleotides encoding the polypeptides of Claim 1, vectors and host cells comprising said polynucleotides, and methods of producing said polypeptides, Claims 11, 13-16, 19, and 20 are also rejected under 35 U.S.C. 112 first paragraph due to lack of enablement for the same reasons discussed above.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of polypeptides with an enormous number of amino acid modifications of the polypeptide of SEQ ID NO: 1 and the encoding polynucleotides. The

scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of sequences having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Written Description

Claims 1-4, 8-11, 13-16, 19, and 20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Claims 1-4 and 8-10 are directed to a genus of polypeptides comprising all variants of SEQ ID NO: 1, having any structure comprising a substitution at Ile¹⁷, and having melavonate kinase activity with decreased feedback sensitivity. The specification teaches the structure of only a single representative species of such polypeptides. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of being a variant of SEQ ID NO: 1, having any structure comprising a substitution at Ile¹⁷, and having melavonate kinase activity with decreased feedback sensitivity. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Since Claims 11, 13-16, 19, and 20 further recite polynucleotides encoding the polypeptides of Claim 1, vectors and host cells comprising said polynucleotides, and methods of

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producing said polypeptides, Claims 11, 13-16, 19, and 20 are also rejected under 35 U.S.C. 112 first paragraph due to lack of enablement for the same reasons discussed above.

Allowable Subject Matter

No claims are allowable.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

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system, see <http://pair-direct.uspto.gov>. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Art Unit 1652



SHERIDAN SWOPE, PH.D.
PRIMARY EXAMINER